February 1, 1996 (now U.S. Patent No. 5,773,571), which claims priority to Serial No. 08/054,363, filed April 26, 1993 (now U.S. Patent No. 5,539,082). Since Serial No. 08/054,363, filed April 26, 1993, supports the present claims, and was filed nearly three years before publication of the Thomson reference, this chain of priority effectively removes the Thomson reference as prior art.

In this regard, Applicants respectfully direct the Examiner's attention to the '363 application, now issued as U.S. Patent No. 5,539,082, wherein compounds of Formula I are thoroughly described. Applicants note that the structures of Formula I, set forth at column 3, line 19 of the issued patent, provide more than an adequate basis for the above-mentioned claim of priority.

Indeed, the very features of the Thomson reference that the Office Action has alleged to be relevant, are present in the applications to which Applicants now claim priority. Particularly, the Office Action alleges that the Thomson reference teaches peptide nucleic acids of the present invention when Q is Ri-Rj, R^1 is H, R^3 is R^7, and J is Rh, where J may be -NHLysNH$_2$, Q may be a lipophilic group (such as a steroid), and R^3 may be a variety of groups including side chains of naturally occurring amino acids. Similarly, Applicants' earliest priority document teaches that Rh may be -NH$_2$LysNH$_2$, Q may be a lipophilic group (such as a steroid), and $R^{7'}$ may be side chains of naturally occurring amino acids (*see, e.g.*, the '363 application at column 4, lines 39 to 47, and column 5, lines 16 to 24). Moreover, Applicants' priority document discloses the administration of PNA compounds into the cells of an organism (*see, e.g.*, column 7, lines 1-5).

Thus, Applicants respectfully submit that the priority disclosure of the '383 reference antedates the Thomson reference by showing prior invention of all the relevant disclosure of all relevant subject matter.[1]

Claims 15-17, 25, 26, and 31 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious in view of the combined teachings of the Thomson reference and certain other references. These rejections, however, assume that the Thomson reference is available as prior art. Since, as noted above, this assumption is incorrect, the rejections for alleged obviousness are believed to be improper. Accordingly, Applicants respectfully request reconsideration and withdrawal of the art rejections under 35 U.S.C. §§ 102 and 103.

Claims 23, 24, and 39-52 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Applicants respectfully request reconsideration of this rejection, as there is no reason to believe that one of ordinary skill in the art would not be able to practice the claimed methods and put them to their many uses.

The first paragraph of Section 112 of the patent statute requires only objective enablement of the invention. How an enabling disclosure is set forth, either by the use of specific examples or broad terminology, is of no importance. *In re Marzocchi*, 169 USPQ 367 (C.C.P.A. 1971). When rejecting a claim under the enablement requirement, it is the PTO that

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[1] With similar reasoning, the '571 application (now U.S. Patent No. 5,773,571) discloses a compound of Formula (I) at column 3, line 17 to column 4, lines 48, wherein substituent Q is in an equivalent position to Ri in Formulas (IIIa) and (IIIb) found at the bottom of column 4 and the top of column 5, respectively. Substituent Q is defined as including, but not limited to hydrogen, alkyl, amino protecting groups, reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids, steroids, oligonucleotides, and soluble and insoluble polymers.

bears the initial burden of setting forth a reasonable explanation as to why he believes that the scope of protection is not adequately enabled. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). Accordingly, to properly assert a rejection on the grounds that the disclosure is not enabling, the Office Action must provide evidence or sound technical reasoning substantiating its position. As the court noted in *In re Armbruster*, 512 F.2d 676, 677 (C.C.P.A. 1975) the PTO not only must "explain why it doubts the truth or accuracy of any statements in a supporting disclosure" but must also "back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement."

The Office Action does not provide sufficient reasoning to doubt that the present claims are enabled. Instead, the Office Action erroneously suggests that the skilled artisan would be required to overcome well-known, unsolved problems to practice the claimed invention. Applicants are further criticized for not addressing these problems by, among other things, providing guidance to teach "the effective delivery of the peptide nucleic acid in a whole organism." Applicants respectfully submit that they are under no obligation to do so. In any event, even assuming that Applicants were required to overcome these obstacles (which they are not), the Office Action fails to establish that these problems are so severe that they would prohibit obtaining at least some measurable results.

The Office Action notes that Rojanasakul, *Advanced Drug Delivery Reviews*, 18, 115-131 (1996) ("the Rojanasakul reference") and Gewirtz, *Facilitating oligonucleotide delivery: Helping antisense deliver on its promise*, *Proc. Natl. Acad. Sci.*, Vol. 93, pp. 3161-3163 (1996) (the

Gewirtz reference) disclose certain "problems" that allegedly would be encountered in the therapeutic use of oligonucleotides. These disclosures, however, are not believed to adequately support rejection of the claims for alleged lack of enablement. What the present Office Action fails to appreciate is that these references nowhere suggest that those skilled in the art would not be able to practice the claimed invention at all. Although the Office Action contends that these references allege that pharmacological delivery of oligonucleotides is something that "must be addressed," this is only in connection with the feasibility of the disclosed compounds as commercial products. There is, however, no requirement *in the patent laws* that patentable inventions be problem-free, much less that they be problem-free in a commercial setting. In this regard, the Examiner has pointedly failed to demonstrate that any of the "problems" disclosed by the cited references are so significant as to entirely impede practice of the claimed methods.

The Office Action also fails to consider the entirety of the cited disclosures. For example, the Rojanasakul reference suggests that his alleged "problems" would not, in fact, impede practice of the claimed methods. To the contrary, the Rojanasakul reference states that compounds such as those recited in the claims show great promise:

> [s]everal ON drugs have already demonstrated enough promise to justify clinical trials. They are being tested in patients suffering from leukemia, AIDS, and other diseases in which improved treatments are necessary. It is expected that in the future these ON drugs will be commonly used to treat those diseases for which no effective therapies yet exist.

See, the Rojanasakul reference at page 126.

Similarly, the Gewirtz reference makes clear that oligonucleotide technology is readily

applied, stating that "[a]ntisense technology has received the majority of the attention because of their apparent ***ease of synthesis and use***." *See*, the Gewirtz reference at page 3161 (emphasis added). These passages serve as compelling evidence that the state of the art of oligonucleotide therapeutics, at the time the present application was filed, was such that an artisan could readily obtain at least some measurable test results once armed with the teachings of the present application.

Not only does the mere existence of problems associated with the claimed inventions not negate their patentablility, but such problems are to be expected. It is well-established that pharmaceutical inventions usually require further research and development. *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995). Were such inventions not patentable long before being optimized or ready for human use, the incentive to fully research and develop vital drugs and potential cures would be completely removed. *Id.* at 1567-68.

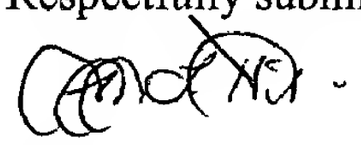
With regard to the suggestion that "reasonable working examples that reasonably correlate with the claimed embodiment are considered to be absent from the specification" (*See* Office Action mailed August 2, 2000 at page 22), Applicants respectfully submit that an application cannot be deemed silent as to certain embodiments simply because they are not set forth as working examples. Only an enabling disclosure is required. M.P.E.P. § 2164.02. The Office Action's characterization misinterprets the present invention in an effort to limit its scope, and fails to consider the genus as a whole, as is required by law. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). In any event, mere statements as to the absence of additional working examples

is insufficient to compel a conclusion of nonenablement, even in the unpredictable arts. *In re Colianni*, 668 F.2d 1229 (C.C.P.A. 1982).

Thus, the Office Action's contentions as to alleged difficulties that those skilled in the art would encounter in practicing the claimed inventions simply do not constitute evidence or technical reasoning of the sort required to substantiate allegations that there is a lack of enablement. To the extent that "problems" are identified in the references cited in the Office Action, such "problems" relate to optimizing the performance of a therapeutic product for clinical use. Because there is no requirement that Applicants optimize an invention for it to be patentable, there is no basis for the rejection for lack of enablement. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

Applicants submit that the foregoing constitutes a full and complete response to the Office Action of record, and that claims 15-52 are in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



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